

BEST AVAILABLE COPY

Serial No. 10/754,923

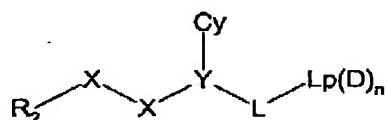
Response to Office Action of November 26, 2004

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1 (previously presented): A serine protease inhibitor compound of formula (I)



(I)

wherein:

R_2 is:-

(i) phenyl optionally being substituted in the 3 and/or 4 position by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO_2- or R_1 , and optionally substituted at the 6 position by amino, hydroxy, halo, alkyl, carboxy, alkoxy carbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio;

(ii) naphth-2-yl optionally substituted at the 6 or 7 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j} and optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio;

(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by halo, haloalkoxy,

Serial No. 10/754,923

Response to Office Action of November 26, 2004

haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j};

(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;

(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j};

(vi) 3,4-methylenedioxypyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;

(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;

(viii) pyrazol-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j};

(ix) pyrid-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j};

(x) pyrid-3-yl optionally substituted at the 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j};

(xi) benzofur-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j};

(xii) indol-2-yl optionally substituted on the indole nitrogen atom by alkyl and optionally substituted at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j};

(xiii) indol-6-yl substituted at the 5 position by amino, hydroxy, halo, alkyl, carboxy, alkoxy carbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio and optionally substituted at

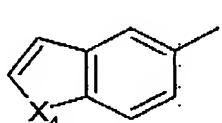
Serial No. 10/754,923

Response to Office Action of November 26, 2004

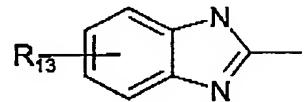
the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j}; or

(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j};

with the proviso that R₂ cannot be aminoisoquinolyl; or R₂ is a group of formula (F') or (H')



(F)



or

(H')

wherein X₄ is O or S, and R₁₃ is selected from hydrogen, fluoro, chloro and methyl;

-X-X- is -CONH-;

R₁ is hydrogen, hydroxy, alkoxy, alkyl, alkylaminoalkyl, alkanoyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkylamino, carboxyl, carboxymethyl, amido or amidomethyl;

R_{1j} is hydrogen, hydroxy, alkoxy, alkyl, alkanoyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylamino, carboxyl, carboxymethyl, amido or amidomethyl;

Y (the α-atom) is a CH group;

Cy is an optionally R_{3a} substituted: phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl, furanyl, pyrrolyl, isoxazolyl, isothiazolyl; pyrazolyl, oxazolyl, imidazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, pyrimidinyl, pyridazinyl, quinolyl, isoquinolyl, benzofuryl, benzothienyl or cycloalkyl group, or a phenyl group substituted by R_{3i}X_i;

Serial No. 10/754,923
 Response to Office Action of November 26, 2004

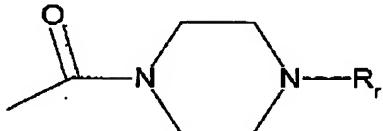
each R_{3a} independently is hydrogen, hydroxyl, alkoxy, aralkyloxy, alkyl, alkylaminoalkyl, hydroxymethyl, carboxy, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, aminomethyl, CONH₂, CH₂CONH₂, (1-6C) alkanoylamino, alkoxy carbonylamino, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkylimidazolyl, thiazolyl, alkylthiazolyl, alkylloxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, haloalkyl, a group of the formula -C(X³)N(R¹¹)R¹² (wherein X³ is O or S; and R¹¹ and R¹² are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group), or -OCH₂O- which is bonded to two adjacent ring atoms in Cy;

X_i is a bond, O, NH or CH₂;

R_{3i} is phenyl, pyridyl or pyrimidinyl optionally substituted by R_{3a};

and

-L-L_p(D)_n is of the formula:



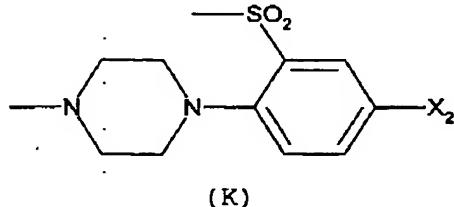
in which R_x is -(CH₂)_c-R_C, -CHReR_f, -CH₂-CHReR_f, -CH₂-CH₂-CHReR_f, or R_g in which c is 1 or 2; R_C is thiienyl, thiazolyl (which may bear an amino substituent), isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, pyridyl (which may bear an alkylsulphonyl, aminosulphonyl, alkylaminosulphonyl, alkylaminocarbonyl, amino, amido, (1-4C) alkoxy carbonyl, carboxy, acetyl amino, chloro, fluoro, cyano, (1-3C) alkyl, trifluoromethyl, methoxy, ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl or tetrazolyl substituent), pyrimidinyl, pyridazinyl, pyrazinyl or phenyl

Serial No. 10/754,923

Response to Office Action of November 26, 2004

(which may bear a methyl, methylamino, dimethylamino, carboxy, dialkylaminosulphonyl, alkylsulphonyl, aminosulphonyl, alkylaminosulphonyl, alkylaminocarbonyl, amino, amido, alkoxy carbonyl, acetyl amino, chloro, fluoro, cyano, methoxy, ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl or tetrazolyl substituent); each of R_e and R_f independently is hydrogen or C₁-3alkyl; or CHR_eR_f is cyclopentyl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 3- or 4-position), cyclohexyl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 1-position), piperidin-4-yl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 1-position), or indan-2-yl; and R_g is 2-methylsulphonylphenyl which may bear a 4-fluoro substituent or R_g is λ⁶-1,1-dioxobenzo[b]thiophen-7-yl;

or a physiologically-tolerable salt thereof;
provided that Lp(D)_n is not of the formula (K):



wherein X₂ is fluoro or hydrogen.

2 (previously presented): A compound according to claim 1

Serial No. 10/754,923
Response to Office Action of November 26, 2004

wherein:

R₂ is:-

(i) phenyl optionally being substituted in the 3 and/or 4 position by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO₂- or R₁, and optionally substituted at the 6 position by amino, hydroxy, halo, alkyl, carboxy, alkoxy carbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio;

(ii) naphth-2-yl optionally substituted at the 6 or 7 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j} and optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio;

(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j};

(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;

(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R₁;

(vi) 3,4-methylenedioxophenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;

(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;

(viii) pyrazol-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R₁;

Serial No. 10/754,923
Response to Office Action of November 26, 2004

(ix) pyrid-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R₁;

(x) pyrid-3-yl optionally substituted at the 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R₁;

(xi) benzofur-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j};

(xii) indol-2-yl optionally substituted on the indole nitrogen atom by alkyl and optionally substituted at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j};

(xiii) indol-6-yl substituted at the 5 position by amino, hydroxy, halo, alkyl, carboxy, alkoxy carbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio and optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j}; or

(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j};

with the proviso that R₂ cannot be aminoisoquinolyl;

Cy is an optionally R_{3a} substituted phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl or cycloalkyl group; each R_{3a} independently is hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl,

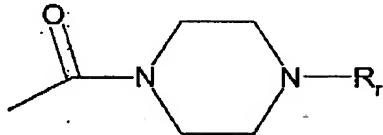
Serial No. 10/754,923

Response to Office Action of November 26, 2004

aminomethyl, CONH₂, CH₂CONH₂, acetylamino,
methoxycarbonylamino, ethoxycarbonylamino, t-
butoxycarbonylamino, amino, fluoro, chloro, cyano, nitro,
thiol, methylthio, methylsulphonyl, ethylsulphonyl,
methylsulphenyl, methylsulphonylamido, ethylsulphonylamido,
methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl,
trifluoromethoxy or trifluoromethyl;

and

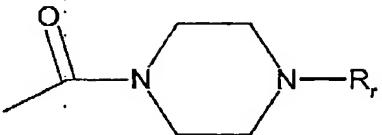
-L-Lp(D)_n is of the formula:



in which R_f is -(CH₂)_c-R_C, -CHR_eR_f, -CH₂-CHReR_f, or R_g in
which c is 1 or 2; R_C is pyridyl or phenyl (which phenyl may
bear a fluoro, chloro, methyl, CONH₂, SO₂NH₂,
methylaminosulphonyl, dimethylaminosulphonyl, methoxy or
methylsulphonyl substituent); each of R_e and R_f independently
is hydrogen or C₁₋₃alkyl; or CHR_eR_f is cyclopentyl (which may
bear a methyl, ethyl or hydroxymethyl substituent at the 3- or
4-position), cyclohexyl (which may bear a methyl, ethyl or
hydroxymethyl substituent at the 3- or 4-position),
tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-
yl (which may bear a 1-methyl substituent), piperidin-4-yl
(which may bear a 1-methyl substituent) or indan-2-yl; and R_g
is 2-methylsulphonylphenyl which may bear a 4-fluoro
substituent or R_g is λ^{6-1,1-dioxobenzo[b]thiophen-7-yl.}

3 (original): A compound according to claim 1 wherein
-L-Lp(D)_n is of the formula:

Serial No. 10/754,923
 Response to Office Action of November 26, 2004



in which R_x is -(CH₂)_c-R_c; in which c is 2; R_c is thiaryl, thiazolyl (which may bear an amino substituent), isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, pyridyl (which may bear an amino, methoxycarbonyl, carboxy, fluoro, cyano, methyl, methylsulphonyl, aminosulphonyl, methylaminosulfonyl, dimethylaminosulfonyl, or trifluoromethyl substituent), pyrimidinyl, pyridazinyl, pyrazinyl or phenyl (which phenyl may bear a fluoro, chloro, cyano, methyl, amino, methylsulphonyl, aminosulphonyl, methylaminosulphonyl, dimethylaminosulphonyl, methylamino, dimethylamino, carboxy, methoxycarbonyl or methoxy substituent).

4 (previously presented): A compound according to claim 3 wherein R_c is thiazolyl (which may bear an amino substituent), pyrimidinyl, pyrazolyl, imidazolyl, pyridyl (which may bear a methylsulphonyl, aminosulphonyl, methylaminosulfonyl, dimethylaminosulfonyl, fluoro, cyano, methyl or trifluoromethyl substituent), pyridazinyl, pyrazinyl or phenyl (which phenyl may bear a fluoro, chloro, cyano, methyl, amino, methylamino, dimethylamino, carboxy, methoxycarbonyl, methylsulphonyl, aminosulphonyl, methylaminosulfonyl, dimethylaminosulfonyl, or methoxy substituent).

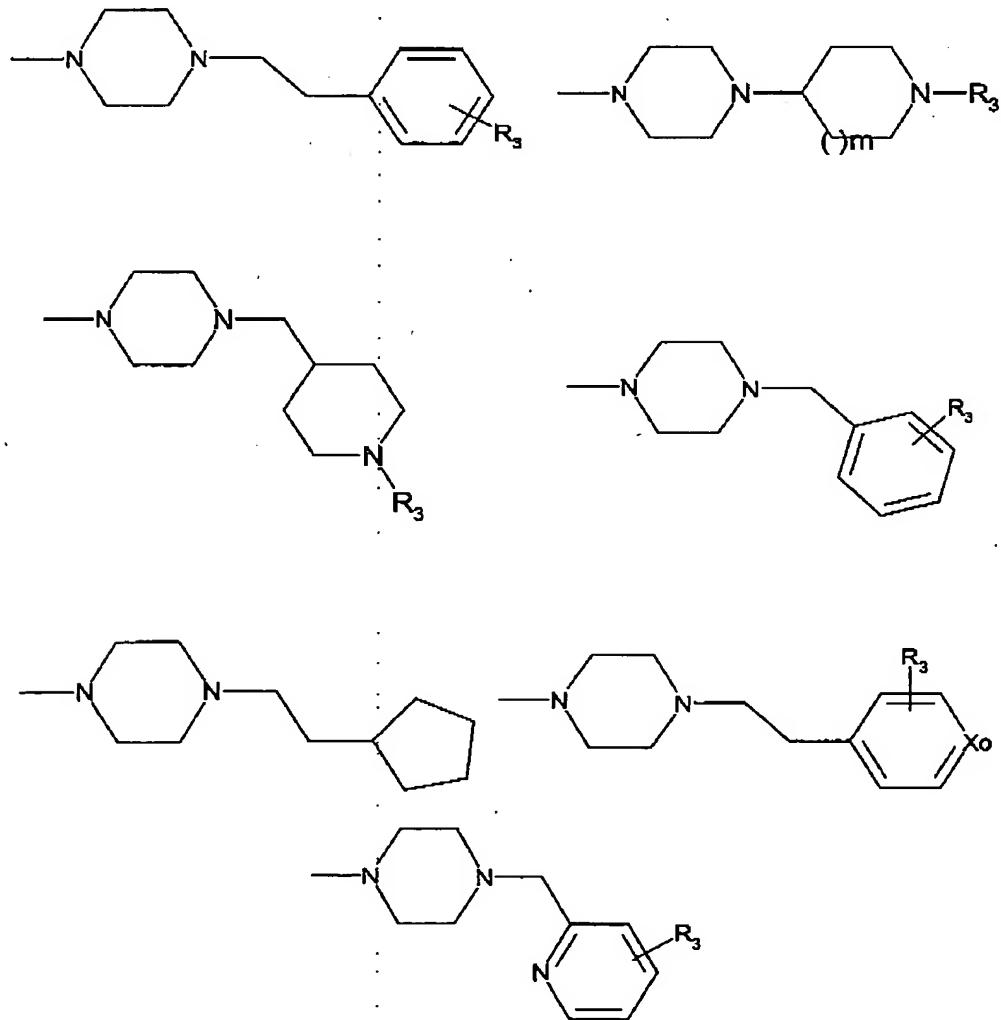
5 (previously presented): A compound according to claim 4 wherein R_c is thiazolyl (which may bear an amino substituent), pyrazolyl, imidazolyl, pyridyl (which may bear a fluoro, cyano, methyl or trifluoromethyl substituent), pyridazinyl or pyrazinyl.

Serial No. 10/754,923

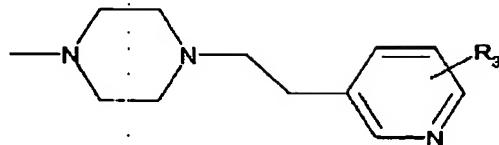
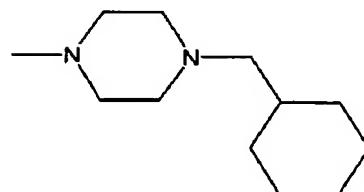
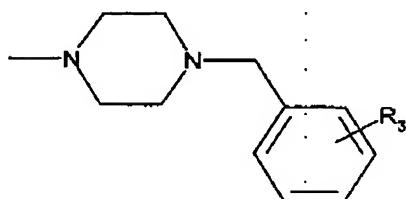
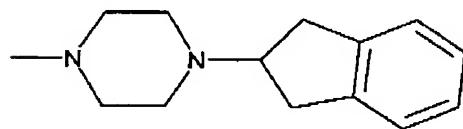
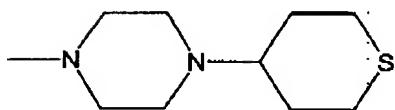
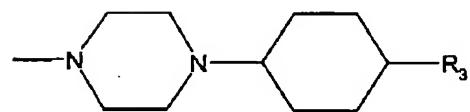
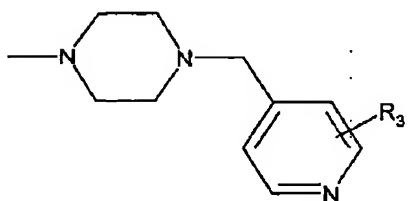
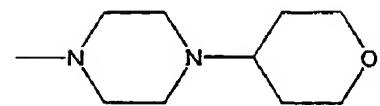
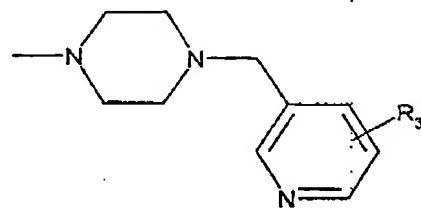
Response to Office Action of November 26, 2004

6 (previously presented): A compound according to claim 5 wherein R_c is thiazol-2-yl, 2-aminothiazol-4-yl, pyrazol-1-yl, pyrazol-4-yl, pyridazin-3-yl, imidazol-1-yl, imidazol-4-yl, pyrazin-2-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, 3-fluoropyrid-4-yl, 2-cyanopyrid-4-yl, 2-methylpyrid-4-yl or 2-trifluoromethylpyrid-6-yl.

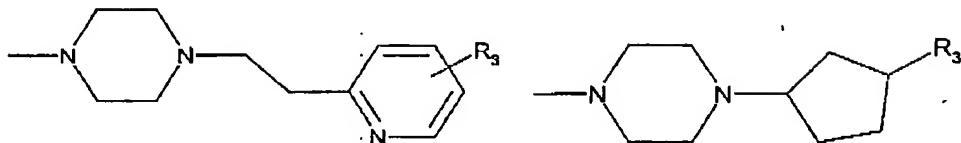
7 (currently amended): A compound according to claim 1 wherein L is CO and -L_p(D)_n is of the formula:



Serial No. 10/754,923
Response to Office Action of November 26, 2004



Serial No. 10/754,923
 Response to Office Action of November 26, 2004



wherein;

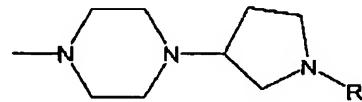
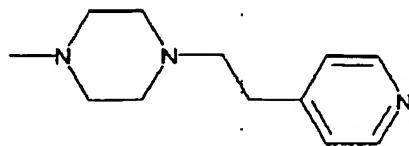
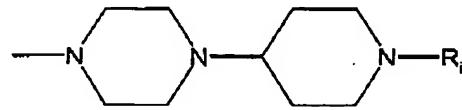
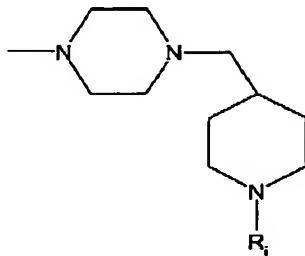
m represents 0 or 1;

Xo \neq represents CH or N; and

when R₃ is present as a substituent on an aromatic ring, it is selected from hydrogen, alkylsulphonyl, aminosulphonyl, alkylaminosulphonyl, alkylaminocarbonyl, amino, amido, alkoxy carbonyl, acetyl amino, chloro, fluoro, cyano, methoxy, ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl and tetrazolyl; and

when R₃ is present as a substituent on a saturated ring, it is selected from hydrogen, hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl and ethoxycarbonyl.

8 (currently amended): A compound according to claim 7 wherein -Lp(D)_n is of the formula:



wherein R₁ is hydrogen, methyl or ethyl or (1-6C)alkyl.

Serial No. 10/754,923

Response to Office Action of November 26, 2004

9 (previously presented): A compound according to claim 1 wherein R₂ is:-

(i) phenyl optionally being substituted in the 3 and/or 4 position by fluoro, chloro, bromo, iodo, nitro, difluoromethoxy, trifluoromethoxy, amino, cyano, trifluoromethyl, methylthio, vinyl, carboxy, acetoxy, MeSO₂-, hydroxy, methoxy, ethoxy, methyl, methoxycarbonyl, methylamino, ethylamino or amido, and optionally substituted at the 6 position by amino, hydroxy, fluoro, methoxycarbonyl, cyano or aminomethyl;

(ii) naphth-2-yl optionally substituted at the 6, position by hydroxy and optionally substituted at the 3 position by amino or hydroxy;

(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by chloro, bromo, amino, methyl or methoxy;

(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;

(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by methylthio, methyl or acetyl;

(vi) 3,4-methylenedioxophenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;

(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;

(viii) pyrazol-2-yl substituted at the 5 position by methyl;

(ix) 5-chloropyrid-2-yl;

(x) pyrid-3-yl or 6-chloropyrid-3-yl;

(xi) benzofur-2-yl, 5-chlorobenzofur-2-yl, 3-methylbenzofur-2-yl, 5-methylbenzofur-2-yl or 6-methoxybenzofur-2-yl; (xii) indol-2-yl optionally substituted on the indole nitrogen atom by methyl and optionally

Serial No. 10/754,923

Response to Office Action of November 26, 2004

substituted at the 5 or 6 position by fluoro, chloro, bromo, methyl or methoxy;

(xiii) indol-6-yl substituted at the 5 position by chloro, fluoro or hydroxy and optionally substituted at the 3 position by chloro or methyl; or

(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by fluoro, chloro or methyl, and optionally substituted at the 5 or 6 position by fluoro, chloro, methyl, hydroxy, or methoxy.

10 (previously presented): A compound according to claim 9 wherein R₂ is:-

(i) phenyl, 2-aminophenyl, 3-aminophenyl, 2-amino-4-fluorophenyl, 2-amino-4-chlorophenyl, 2-amino-4-nitrophenyl, 2-amino-4-methylphenyl, 3,4-diaminophenyl, 3-amino-4-fluorophenyl, 3-amino-4-chlorophenyl, 3-amino-4-bromophenyl, 3-amino-4-hydroxyphenyl, 3-amino-4-carboxymethylphenyl, 3-amino-4-methylphenyl, 3-amino-4-methoxyphenyl, 2-fluorophenyl, 4-fluoro-3-cyanophenyl, 3-chlorophenyl, 3-chloro-4-hydroxyphenyl, 4-chlorophenyl, 4-chloro-2-hydroxyphenyl, 4-chloro-3-hydroxyphenyl, 4-chloro-3-methylphenyl, 4-chloro-3-methoxyphenyl, 4-bromophenyl, 4-bromo-3-methylphenyl, 4-iodophenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2-hydroxyphenyl, 2-hydroxy-4-methoxyphenyl, 3-hydroxyphenyl, 3-hydroxy-4-methylphenyl, 2,4-dihydroxyphenyl, 3,4-dihydroxyphenyl, 3-hydroxy-4-methoxyphenyl, 4-difluoromethoxyphenyl, 4-trifluoromethoxyphenyl, 4-trifluoromethylphenyl, 4-methylthiophenyl, 4-methoxycarbonylphenyl, 4-acetoxyphenyl, 4-methanesulfonylphenyl, 3-methylphenyl, 4-methylphenyl, 4-vinylphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 4-methoxy-3-chlorophenyl, 4-methoxy-3-methylphenyl, 3-methylaminophenyl, 4-methylaminophenyl, 4-ethylaminophenyl or 2-aminomethylphenyl;

Serial No. 10/754,923

Response to Office Action of November 26, 2004

(ii) naphth-2-yl, 3-aminonaphth-2-yl, 3-hydroxynaphth-2-yl or 6-hydroxynaphth-2-yl;

(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, 3-chloroindol-6-yl, 3-bromoindol-6-yl, 3-methylindol-6-yl, 3-methoxyindol-6-yl, indazol-5-yl, 3-aminoindazol-5-yl, indazol-6-yl, benzothiazol-6-yl, 3-aminobenzisoxazol-5-yl;

(iv) benzimidazol-5-yl, 2-aminobenzimidazol-5-yl, or benzothiazol-6-yl;

(v) thien-2-yl, 5-methylthien-2-yl, 5-methylthio-thien-2-yl, 5-acetylthien-2-yl or thien-3-yl;

(vi) 3,4-methylenedioxypyhenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;

(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;

(viii) 5-methylpyrazol-2-yl;

(ix) 5-chloropyrid-2-yl;

(x) pyrid-3-yl, 6-chloropyrid-3-yl;

(xi) benzofur-2-yl, 5-chlorobenzofur-2-yl, 3-methylbenzofur-2-yl, 5-methylbenzofur-2-yl, 6-methoxybenzofur-2-yl;

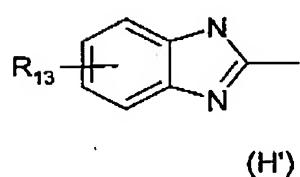
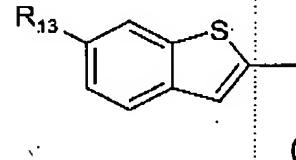
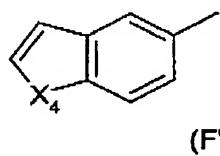
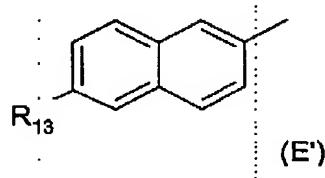
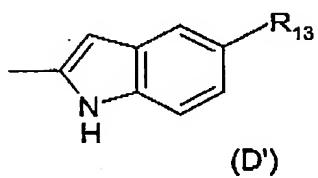
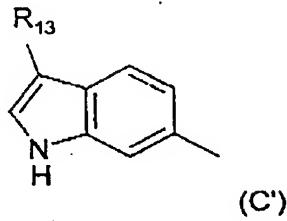
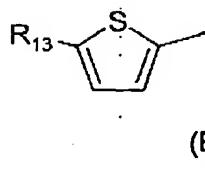
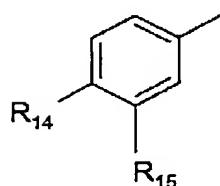
(xii) indol-2-yl, 5-fluoroindol-2-yl, 5-chloroindol-2-yl, 5-methylindol-2-yl, 5-methoxindol-2-yl, 6-methoxyindol-2-yl and 1-methyl-indol-2-yl;

(xiii) 5-fluoroindol-6-yl; or

(xiv) benzo[b]thiophen-2-yl, 5-chloro- benzo[b]thiophen-2-yl or 6-chlorobenzo[b]thiophen-2-yl.

11 (previously presented): A compound according to claim 1 wherein R₂ is selected from one of the formula (A') to (H'):

Serial No. 10/754,923
 Response to Office Action of November 26, 2004



wherein X₄ is O or S, R₁₃ is selected from hydrogen, fluoro [except for (C')], chloro or methyl and R₁₄ is selected from hydrogen, methyl, ethyl, fluoro, chloro, and methoxy and R₁₅ is selected from hydrogen, methyl, fluoro, chloro and amino.

12 (previously presented): A compound according to claim 11, wherein R₂ is 4-chlorophenyl, 4-methoxyphenyl, 3-amino-4-chlorophenyl, indol-2-yl, 5-chloroindol-2-yl, indol-6-yl, 3-chloroindol-6-yl or 3-methylindol-6-yl.

Serial No. 10/754,923
Response to Office Action of November 26, 2004

13 (canceled) :

14 (canceled) :

15 (canceled) :

16 (canceled) :

17 (canceled) :

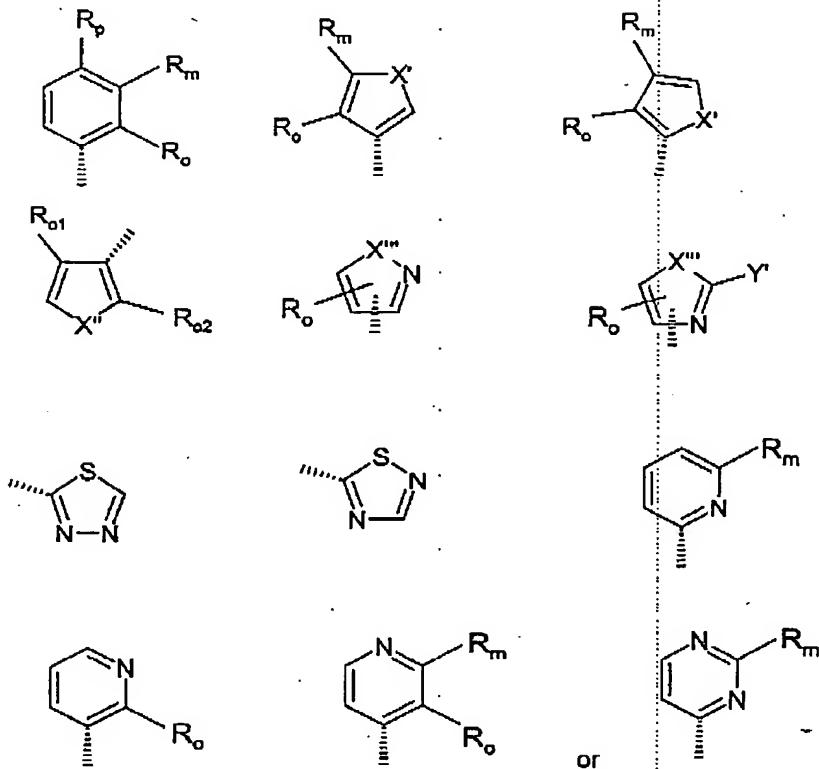
18 (canceled) :

19 (previously presented) : A compound according to claim 1 wherein R_{3a} is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl, CONH₂, CH₂CONH₂, acetyl amino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, bromo, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy, trifluoromethyl, bromo, -OCH₂O- (which is bonded to two adjacent ring atoms in Cy) and -C(X³)N(R¹¹)R¹² (wherein X³ is O or S and R¹¹ and R¹² are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group).

20 (canceled) :

Serial No. 10/754,923
 Response to Office Action of November 26, 2004

21 (previously presented): A compound according to claim 1 wherein Cy is selected from:



wherein:

X' is selected from O, S and NMe;

X'' is selected from O and S;

X''' is selected from O, S, NH and NMe;

Y' is selected from hydrogen, amino and methyl;

R_o is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphanyl and methylsulphonyl;

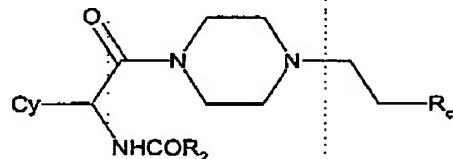
R_m is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphanyl, methylsulphonyl, carboxy, methoxycarbonyl and a group of the

Serial No. 10/754,923
 Response to Office Action of November 26, 2004

formula -C(X³)N(R¹¹)R¹² (wherein X³ is O or S and R¹¹ and R¹² are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group); R_P is selected from hydrogen and fluoro; or R_O and R_M or R_M and R_P form an -OCH₂O- group; or R_O and R_M together with the ring to which they are attached form a 5 or 6 membered aryl or heteroaryl ring (wherein the heteroaryl ring contains 1 or 2 heteroatoms selected from nitrogen, oxygen and sulfur); and one of R_{O1} and R_{O2} is hydrogen and the other is R_O.

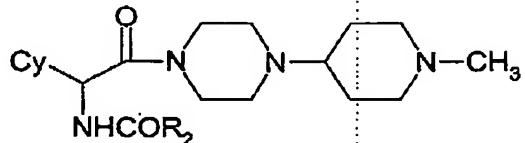
22 (previously presented): A compound according to claim 1 wherein Cy is selected from phenyl, 2-chlorophenyl, 2-methoxyphenyl, 4-carbamoylphenyl, pyrid-2-yl, pyrid-4-yl, thien-2-yl, thien-3-yl, furan-2-yl, furan-3-yl, imidazol-2-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl and quinolin-4-yl.

23 (previously presented): A compound of the formula:



wherein Cy, R₂ and R_c are as defined in any one of claims 1 to 6, 9 to 12, 19 and 21 to 22.

24 (previously presented): A compound of the formula:



Serial No. 10/754,923

Response to Office Action of November 26, 2004

wherein Cy and R₂ are as defined in any one of claims 1 to 2, 9 to 12, 19 and 21 to 22.

25 (canceled):

26 (previously presented): A compound as claimed in Claim 1, which is selected from:

1-(Indole-6-carbonyl-D-phenylglycinyl)-4-[2-(4-pyridinyl)-ethyl]piperazine;
1-(3-Chloroindole-6-carbonyl-D-phenylglycinyl)-4-[2-(4-pyridinyl)ethyl]piperazine;
1-(4-Methoxybenzoyl-D-phenylglycinyl)-4-(1-methylpiperidin-4-yl)piperazine;
1-(4-Methoxybenzoyl-D-(2-chlorophenyl)glycinyl)-4-(1-methylpiperidin-4-yl)piperazine;
1-(Indole-6-carbonyl-D-(2-chlorophenyl)glycinyl)-4-(1-methylpiperidin-4-yl)piperazine; and
1-(4-Methoxybenzoyl-D-(2-trifluoromethylphenyl)glycinyl)-4-(1-methylpiperidin-4-yl)piperazine;
and physiologically-tolerable salts thereof.

27 (previously presented): A pharmaceutical composition, which comprises a compound as claimed in claim 1 together with at least one pharmaceutically acceptable carrier or excipient.

28 (canceled):

29 (canceled):

30 (previously presented): A method of treatment of a human or non-human animal body to combat a thrombotic disorder selected from venous thrombosis, pulmonary embolism, arterial thrombosis, myocardial ischaemia, myocardial infarction and

Serial No. 10/754,923

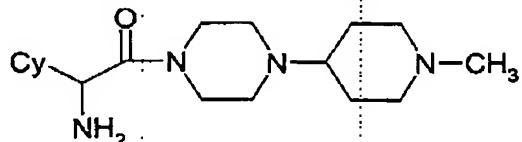
Response to Office Action of November 26, 2004

cerebral thrombosis, which comprises administering to said body an effective amount of a compound as claimed in claim 1.

31 (canceled):

32 (canceled):

33 (previously presented): A compound of the formula



or a salt thereof in which Cy is as defined in any one of claims 1, 21 and 22.

34 (previously presented): A compound as claimed in any one of claims 1 to 1213, 19 and 21 to 22, wherein the alpha atom in Y is carbon and has the conformation that would result from construction from a D- α -aminoacid $\text{NH}_2\text{-CH}(\text{Cy})\text{-COOH}$ where the NH_2 represents part of X-X.

35 (previously presented): A pharmaceutical composition, which comprises a compound as claimed in claim 34 together with at least one pharmaceutically acceptable carrier or excipient.

36 (previously presented): A method of treatment of a human or non-human animal body to combat a thrombotic disorder selected from venous thrombosis, pulmonary embolism, arterial thrombosis, myocardial ischaemia, myocardial infarction and cerebral thrombosis, which comprises administering to said body an effective amount of a compound as claimed in claim 34.

37 (previously presented): A method as claimed in claim 36 in which said human or non-human animal body is a human body.

Serial No. 10/754,923
Response to Office Action of November 26, 2004

38 (new) A compound as claimed in claim 33, in which the carbon atom bearing Cy has the conformation that would result from construction from a D- α -aminoacid NH₂-CH(Cy)-COOH.

39 (new) A compound as claimed in claim 38, in which Cy is a phenyl group.

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- BLACK BORDERS**
- IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- FADED TEXT OR DRAWING**
- BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- SKEWED/SLANTED IMAGES**
- COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- GRAY SCALE DOCUMENTS**
- LINES OR MARKS ON ORIGINAL DOCUMENT**
- REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.